Membrane biophysics define neuron and astrocyte progenitors in the neural lineage.

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Public Summary:
Neural stem and progenitor cells (NSPCs) are a mixture of stem cells and more specialized cells termed progenitors that form the final cells of the brain and spinal cord - neurons, astrocytes and oligodendrocytes. Accurately identifying and characterizing the different progenitor cells in this lineage has continued to be a challenge for the field. We found previously that populations of NSPCs with more neuron progenitors (NPs) can be distinguished from those with more astrocyte progenitors (APs) by their inherent cell membrane properties, without the need for specific cell markers or labels. Here we hypothesize that inherent properties are by themselves sufficient to define NPs and APs and test this by determining whether isolation of cells solely by these properties specifically separates NPs and APs. We found NPs and APs are enriched in distinct fractions after separation by their inherent cell membrane properties. A single round of isolation provided greater NP enrichment than sorting with a traditional NP marker. We tested whether molecules on the cell surface influenced the cell type specific inherent properties and found that sugar molecules on the membrane specifically affected these properties. Inherent cell membrane properties are thus sufficient to define progenitor cells that form neurons and astrocytes in the nervous system, can be used to specifically isolate these cells, and are linked to patterns of sugar molecules on the cell surface.

Scientific Abstract:
Neural stem and progenitor cells (NSPCs) are heterogeneous populations of self-renewing stem cells and more committed progenitors that differentiate into neurons, astrocytes and oligodendrocytes. Accurately identifying and characterizing the different progenitor cells in this lineage has continued to be a challenge for the field. We found previously that populations of NSPCs with more neurogenic progenitors (NPs) can be distinguished from those with more astrogenic progenitors (APs) by their inherent biophysical properties, specifically the electrophysiological property of whole cell membrane capacitance, which we characterized with dielectrophoresis (DEP). Here we hypothesize that inherent electrophysiological properties are sufficient to define NPs and APs and test this by determining whether isolation of cells solely by these properties specifically separates NPs and APs. We found NPs and APs are enriched in distinct fractions after separation by electrophysiological properties using DEP. A single round of DEP isolation provided greater NP enrichment than sorting with PSA-NCAM, which is considered an NP marker. Additionally, cell surface N-linked glycosylation was found to significantly affect cell fate-specific electrophysiological properties, providing a molecular basis for the cell membrane characteristics. Inherent plasma membrane biophysical properties are thus sufficient to define progenitor cells of differing fate potential in the neural lineage, can be used to specifically isolate these cells, and are linked to patterns of glycosylation on the cell surface. Stem Cells 2013.